

**TOXICOLOGICAL PROFILE FOR
ETHYLENE GLYCOL AND PROPYLENE GLYCOL**

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

September 1997

DISCLAIMER

The use of company or product name(s) is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry.

UPDATE STATEMENT

A Technical Report for ethylene glycol and propylene glycol was released in May 1993. This edition supersedes any previously released draft or final profile or report.

Toxicological profiles are revised and republished as necessary, but no less than once every three years. For information regarding the update status of previously released profiles, contact ATSDR at:

Agency for Toxic Substances and Disease Registry
Division of Toxicology/Toxicology Information Branch
1600 Clifton Road NE, E-29
Atlanta, Georgia 30333

FOREWORD

This toxicological profile is prepared in accordance with guidelines* developed by the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency (EPA). The original guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary.

The ATSDR toxicological profile succinctly characterizes the toxicologic and adverse health effects information for the hazardous substance described therein. Each peer-reviewed profile identifies and reviews the key literature that describes a hazardous substance's toxicologic properties. Other pertinent literature is also presented, but is described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.


The focus of the profiles is on health and toxicologic information; therefore, each toxicological profile begins with a public health statement that describes, in nontechnical language, a substance's relevant toxicological properties. Following the public health statement is information concerning levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health are identified by ATSDR and EPA.

Each profile includes the following:

- (A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a hazardous substance to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects;
- (B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure that present a significant risk to human health of acute, subacute, and chronic health effects; and
- (C) Where appropriate, identification of toxicologic testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

The principal audiences for the toxicological profiles are health professionals at the Federal, State, and local levels; interested private sector organizations and groups; and members of the public.

This profile reflects ATSDR's assessment of all relevant toxicologic testing and information that has been peer-reviewed. Staff of the Centers for Disease Control and Prevention and other Federal scientists have also reviewed the profile. In addition, this profile has been peer-reviewed by a nongovernmental panel and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.



David Satcher, M.D., Ph.D.
Administrator
Agency for Toxic Substances and
Disease Registry

*Legislative Background

The toxicological profiles are developed in response to the Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) which amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). Section 211 of SARA also amended Title 10 of the U. S. Code, creating the Defense Environmental Restoration Program. Section 2704(a) of Title 10 of the U. S. Code directs the Secretary of Defense to notify the Secretary of Health and Human Services of not less than 25 of the most commonly found unregulated hazardous substances at defense facilities. Section 2704(b) of Title 10 of the U. S. Code directs the Administrator of the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare a toxicological profile for each substance on the list provided by the Secretary of Defense under subsection (b).

CONTRIBUTORS

CHEMICAL MANAGER(S)/AUTHORS(S):

Ed Murray, Ph.D.
ATSDR, Division of Toxicology, Atlanta, GA

Julia George, Ph.D.
Research Triangle Institute, Research Triangle Park, NC

THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

1. Green Border Review. Green Border review assures consistency with ATSDR policy.
2. Health Effects Review. The Health Effects Review Committee examines the health effects chapter of each profile for consistency and accuracy in interpreting health effects and classifying end points.
3. Minimal Risk Level Review. The Minimal Risk Level Workgroup considers issues relevant to substance-specific minimal risk levels (MI&s), reviews the health effects database of each profile, and makes recommendations for derivation of MRLs.
4. Quality Assurance Review. The Quality Assurance Branch assures that consistency across profiles is maintained, identifies any significant problems in format or content, and establishes that Guidance has been followed.

PEER REVIEW

A peer review panel was assembled for ethylene glycol and propylene glycol. The panel consisted of the following members:

1. Dr. Gregory Grauer, Associate Professor, Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, Colorado;
2. Dr. Philip Leber, Private Consultant, Chem-Tox Consulting, Akron, Ohio; and
3. Dr. Kenneth McMartin, Professor, Department of Pharmacology and Therapeutics, Section of Toxicology, Louisiana State University Medical Center, Shreveport, Louisiana.

These experts collectively have knowledge of ethylene glycol and propylene glycol's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(i)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.

CONTENTS

FOREWORD	v
CONTRIBUTORS	vii
PEER REVIEW	ix
LIST OF FIGURES	xv
LIST OF TABLES	xvii
1. PUBLIC HEALTH STATEMENT	1
1.1 WHAT ARE ETHYLENE GLYCOL AND PROPYLENE GLYCOL?	2
1.2 WHAT HAPPENS TO ETHYLENE GLYCOL AND PROPYLENE GLYCOL WHEN THEY ENTER THE ENVIRONMENT?	3
1.3 HOW MIGHT I BE EXPOSED TO ETHYLENE GLYCOL AND PROPYLENE GLYCOL? ..	3
1.4 HOW CAN ETHYLENE GLYCOL AND PROPYLENE GLYCOL ENTER AND LEAVE MY BODY?	4
1.5 HOW CAN ETHYLENE GLYCOL AND PROPYLENE GLYCOL AFFECT MY HEALTH? ..	5
1.6 ARE THERE MEDICAL TESTS TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO ETHYLENE GLYCOL OR PROPYLENE GLYCOL?	6
1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?	6
1.8 WHERE CAN I GET MORE INFORMATION?	7
2. HEALTH EFFECTS	9
2.1 INTRODUCTION	9
2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE	10
2.2.1 Inhalation Exposure	12
2.2.1.1 Death	12
2.2.1.2 Systemic Effects	13
2.2.1.3 Immunological and Lymphoreticular Effects	25
2.2.1.4 Neurological Effects	26
2.2.1.5 Reproductive Effects	26
2.2.1.6 Developmental Effects	27
2.2.1.7 Genotoxic Effects	28
2.2.1.8 Cancer	28
2.2.2 Oral Exposure	28
2.2.2.1 Death	29
2.2.2.2 Systemic Effects	31
2.2.2.3 Immunological and Lymphoreticular Effects	65
2.2.2.4 Neurological Effects	66
2.2.2.5 Reproductive Effects	68
2.2.2.6 Developmental Effects	70

2.2.2.7	Genotoxic Effects	72
2.2.2.8	Cancer	72
2.2.3	Dermal Exposure	73
2.2.3.1	Death	73
2.2.3.2	Systemic Effects	73
2.2.3.3	Immunological and Lymphoreticular Effects	81
2.2.3.4	Neurological Effects	83
2.2.3.5	Reproductive Effects	84
2.2.3.6	Developmental Effects	84
2.2.3.7	Genotoxic Effects	85
2.2.3.8	Cancer	85
2.3	TOXICOKINETICS	85
2.3.1	Absorption	86
2.3.1.1	Inhalation Exposure	86
2.3.1.2	Oral Exposure	86
2.3.1.3	Dermal Exposure	87
2.3.2	Distribution	88
2.3.2.1	Inhalation Exposure	88
2.3.2.2	Oral Exposure	88
2.3.2.3	Dermal Exposure	89
2.3.3	Metabolism	90
2.3.4	Excretion	92
2.3.4.1	Inhalation Exposure	92
2.3.4.2	Oral Exposure	92
2.3.4.3	Dermal Exposure	94
2.3.5	Mechanism of Action	95
2.4	RELEVANCE TO PUBLIC HEALTH	97
2.5	BIOMARKERS OF EXPOSURE AND EFFECT	118
2.5.1	Biomarkers Used to Identify or Quantify Exposure to Ethylene Glycol or Propylene Glycol	119
2.5.2	Biomarkers Used to Characterize Effects Caused by Ethylene Glycol or Propylene Glycol	120
2.6	INTERACTIONS WITH OTHER CHEMICALS	121
2.7	POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	123
2.8	METHODS FOR REDUCING TOXIC EFFECTS	124
2.8.1	Reducing Peak Absorption Following Exposure	124
2.8.2	Reducing Body Burden	125
2.8.3	Interfering with the Mechanism of Action for Toxic Effects	125
2.9	ADEQUACY OF THE DATABASE	127
2.9.1	Existing Information on Health Effects of Ethylene Glycol and Propylene Glycol	127
2.9.2	Identification of Data Needs	131
2.9.3	Ongoing Studies	147
3.	CHEMICAL AND PHYSICAL INFORMATION	151
3.1	CHEMICAL IDENTITY	151
3.2	PHYSICAL AND CHEMICAL PROPERTIES	151

4. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL	155
4.1 PRODUCTION	155
4.2 IMPORT/EXPORT	159
4.3 USE	159
4.4 DISPOSAL	161
5. POTENTIAL FOR HUMAN EXPOSURE	165
5.1 OVERVIEW	165
5.2 RELEASES TO THE ENVIRONMENT	167
5.2.1 Air	169
5.2.2 Water	173
5.2.3 Soil	174
5.3 ENVIRONMENTAL FATE	175
5.3.1 Transport and Partitioning	175
5.3.2 Transformation and Degradation	177
5.3.2.1 Air	177
5.3.2.2 Water	177
5.3.2.3 Sediment and Soil	179
5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT	180
5.4.1 Air	180
5.4.2 Water	181
5.4.3 Sediment and Soil	182
5.4.4 Other Environmental Media	182
5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE	183
5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	184
5.7 ADEQUACY OF THE DATABASE	185
5.7.1 Identification of Data Needs	185
5.7.2 Ongoing Studies	191
6. ANALYTICAL METHODS	193
6.1 BIOLOGICAL SAMPLES	193
6.2 ENVIRONMENTAL SAMPLES	199
6.3 ADEQUACY OF THE DATABASE	203
6.3.1 IDENTIFICATION OF DATA NEEDS	203
6.3.2 Ongoing Studies	204
7. REGULATIONS AND ADVISORIES	205
8. REFERENCES	213
9. GLOSSARY	247
APPENDICES	
A. MINIMAL RISK LEVEL (MRL) WORKSHEETS	A-1
B. USER'S GUIDE	B-1
C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS	C-1

LIST OF FIGURES

2-1	Levels of Significant Exposure to Ethylene Glycol - Inhalation	17
2-2	Levels of Significant Exposure to Propylene Glycol - Inhalation	21
2-3	Levels of Significant Exposure to Ethylene Glycol - Oral	45
2-4	Levels of Significant Exposure to Propylene Glycol - Oral	53
2-5	Metabolic Pathway for Oxidation of Ethylene Glycol	91
2-6	Propylene Glycol Metabolism in Mammals	93
2-7	Existing Information on Health Effects of Ethylene Glycol	128
2-8	Existing Information on Health Effects of Propylene Glycol	129
5-1	Frequency of NPL Sites with Ethylene Glycol Contamination	166
5-2	Frequency of NPL Sites with Propylene Glycol Contamination	168

LIST OF TABLES

2-1	Levels of Significant Exposure to Ethylene Glycol - Inhalation	14
2-2	Levels of Significant Exposure to Propylene Glycol - Inhalation	19
2-3	Levels of Significant Exposure to Ethylene Glycol - Oral	32
2-4	Levels of Significant Exposure to Propylene Glycol - Oral	49
2-5	Levels of Significant Exposure to Ethylene Glycol - Dermal	75
2-6	Levels of Significant Exposure to Propylene Glycol - Dermal	76
2-7	Genotoxicity of Ethylene Glycol <i>In vivo</i>	109
2-8	Genotoxicity of Ethylene Glycol <i>In vitro</i>	110
2-9	Genotoxicity of Propylene Glycol <i>In vitro</i>	117
3-1	Chemical Identity of Ethylene Glycol and Propylene Glycol	152
3-2	Physical and Chemical Properties of Ethylene Glycol and Propylene Glycol	153
4-1	Facilities that Manufacture or Process Ethylene Glycol	157
5-1	Releases to the Environment from Facilities that Manufacture or Process Ethylene Glycol	170
5-2	National Ethylene Glycol Emissions in Different Environmental Media During 1990–1992	172
6-1	Analytical Methods for Determining Ethylene Glycol and Propylene Glycol in Biological Samples	194
6-2	Analytical Methods for Determining Ethylene Glycol and Propylene Glycol in Environmental Samples	200
7-1	Regulations and Guidelines Applicable to Ethylene Glycol	207
7-2	Regulations and Guidelines Applicable to Propylene Glycol	211